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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/980,913	05/21/2002	Ernest Arenas	0380-P02709USO	3833

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EXAMINER	
MCGILLEM, LAURA L	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 04/19/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/980,913	ARENAS ET AL.	
	Examiner	Art Unit	
	Laura McGillem	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 February 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 5-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 5-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *01 November 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

It is noted that in the response filed 2/2/2006, claims 13-69 have been cancelled. Claims 1-3 and 5-12 are under examination.

Information Disclosure Statement

In the response filed 2/2/2006, Applicants have cited Song et al (Nature 2002, Vol. 417, No. 6884, pages 39-44). This reference has not been properly submitted on an Information Disclosure Statement.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3 and 5-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bowen et al in view of Takeshima et al (of record).

This rejection is being maintained for reasons of record in the previous Office Action, mailed 7/29/2005 and for reasons outlined below.

Applicant submits that the rejection of claims 1-3 and 5-12 as *prima facie* obvious in view of the combined disclosure of Bowen and Takeshima et al is invalid because it is based on the erroneous premise that Takeshima et al reads on "co-culturing neural progenitor cells with Type 1 astrocytes of the mesencephalon and inducing a

dopaminergic neuronal fate". Applicant submits that Takeshima et al does not disclose all the features of the present inventive method which, when combined with the features of Bowen would lead to the instant invention. Applicant submits that application of Takeshima et al is invalid because Takeshima et al teaches promotion of survival of cells in primary culture that are already neuronal cells and the claimed invention resides in the novel and unobvious finding that neural stem cells can be induced to adopt a dopaminergic neuronal cell fate as evidenced on page 22 of Takeshima et al. Applicant also submits that Takeshima et al differs from the present invention in at least two ways:

1) the assay taught by Takeshima et al is based on primary dopaminergic neurons and survival promoting effects of Type-1 astrocytes on primary cultures already containing dopaminergic neurons and not immature, multipotent stem or progenitor cells not fated to acquire any specific phenotype;

2) in Takeshima et al astrocytes are employed as a source of neurotrophic factors, while the inventive method employs astrocytes as instructive factors.

Applicant further submits that astrocytes as a source of instructive factors was not supported by the data at the time the invention was filed. Applicant cites Song et al as evidence of similar unexpected findings of instructional factors from astrocytes for hippocampal neurons. Finally, Applicant submits that the rejection of claims 1-3 and 5-12 was done out of impermissible hindsight.

The arguments have been considered but they have not been found to be persuasive because they appear to be primarily focused on the difference between the claimed invention and the teachings of Takeshima et al.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

This rejection is based on the teachings of both Bowen et al and Takeshima et al. While Takeshima et al do use primary cultures in which some of the cells are TH+ (dopaminergic), their observations of inconsistent increases in the percentage of TH+ neurons and marked growth in neuritic growth and branching lead them to suggest that co-culture with astrocytes "promotes the development of TH+ neurons in culture in the short term" (see page 816, right column). Further, Bowen et al use CNS stem cells to express Nurr1 in a method to induce the cells to a dopaminergic phenotype and discloses that co-culturing with ventral mesencephalon astrocytes is useful for increasing survival of dopaminergic neurons. Therefore, it is the combination of the method of Bowen et al to express Nurr1 in neuronal stem cell and the method of Takeshima et al to co-culture developing neurons with astrocytes, that anticipates the claimed method and not the cell culture of Takeshima et al alone.

Applicants argue that the teaching of Takeshima et al differs from the inventive method because in Takeshima et al astrocytes are employed as a source of neurotrophic factors, not instructive factors as in the inventive method. This is not persuasive because, as written, the claims do not distinguish or specify the role of the factors secreted by the astrocytes as instructive or neurotrophic. The specification teaches that Nurr1 does not induce detectable expression of tyrosine hydroxylase (evidence of dopaminergic phenotype) in the C17.2 line. However, the claims do not distinguish the specific roles of Nurr1 or the astrocyte secreted factors. The specification does not specifically teach that the factors secreted by the astrocytes are "instructive" and not neurotrophic.

Applicant submits that astrocytes as a source of instructive factors was not supported by the data at the time the invention was filed. The specification teaches that the "present disclosure provides the first evidence that Type 1 astrocytes are involved in determination of specific neuronal fates" (see page 9, lines 6-9). None of the above assertions and arguments is reflected in the claims. Therefore, the inventive method as claimed is rendered obvious by the teaching of Bowen et al in view of Takeshima et al.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a

reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura McGillem whose telephone number is (571) 272-8783. The examiner can normally be reached on M-F 8:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Laura McGillem, PhD
4/14/2006

DAVID GUZO
PRIMARY EXAMINER